UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,621	12/11/2003	Atul Varadhachary	HO-P02705US2	8531

26271 7590 07/11/2005

FULBRIGHT & JAWORSKI, LLP
1301 MCKINNEY
SUITE 5100
HOUSTON, TX 77010-3095

EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 07/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/733,621	VARADHACHARY ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-22 and 35-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-22 and 35-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

Status of the Claims

2. Claims 1, 3-22 and 35-37 are pending.

Applicants' amendment filed on April 11, 2005 is acknowledged. Applicants' response has been fully considered. Claims 1 and 22 have been amended, claims 2 and 23-34 have been cancelled, and new claims 35-37 have been added. Thus, claims 1, 3-22 and 35-37 are examined.

Withdrawn Claim Rejections - 35 USC § 112

3. The previous rejection of claims 10 and 22 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicant's amendment to the claim, and applicant's response at pages 5-6 of the amendment filed April 11, 2005.

Withdrawn Claim Rejections - 35 USC § 102

4. The previous rejection of claims 1-6, 11-15, 18-22 and 34 under 35 U.S.C. 102(b) as anticipated by Ando *et al.* (U. S. Patent 5,576,299), is withdrawn in view of applicant's amendment to the claim, applicant's cancellation of the claim, and applicant's response at page 6 in the amendment filed April 11, 2005.

5. The previous rejection of claims 2 and 34 under 35 U.S.C. 102(e) as anticipated by Kruzel *et al.* (mistakenly as US 2003/0056067 in the last Office Action, should be US

2003/0096736, filed May 7, 2002), is withdrawn in view of applicant's cancellation of the claim in the amendment filed April 11, 2005.

Withdrawn Claim Rejections - 35 USC § 103(a)

6. The previous rejection of claims 1-4, 8, 9, 11-13, 15, 18-19, 33 and 34 under 35 U.S.C. 103(a) as being unpatentable over by Olmarker *et al.* (WO 02/080891) in view of Hanson *et al.* (WO 00/01730), is withdrawn in view of applicant's amendment to the claim, applicant's cancellation of the claim, and applicant's response at page 7 of the amendment filed April 11, 2005.

Maintained Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Previous rejection of claims 1, 3-7 and 11-22 under 35 U.S.C. 102(e) as being anticipated by Kruzel *et al.* (US 2003/0096736, filed May 7, 2002) is maintained and amended herein.

Kruzel *et al.* teach lactoferrin (LF) tablets containing 95.45 parts dextrose, 2.97 parts bovine LF, and 0.53 parts calcium stearate (a known antacid) or a capsule (25 mg) was administered to patients with multiple sclerosis (MS, a disease of central nervous system, paragraphs [0022], [0023]) in which two tablets of lactoferrin or a capsule were taken orally twice each day (Examples 2, 3, 4; claims 1, 4-6, 11, 14). The reference also indicates human recombinant lactoferrin may be used alone or in combination with bovine lactoferrin (paragraph [0037]; claim 7); and lactoferrin can be administered enteraly (claims 15-17), preferably orally, or parenterally, preferably intravenously (claim 12), in the form of injectable solution, or, as a liposomal formulation such as transdermal patches (claim 13), and a single or twice daily dose of 0.01 mg to 20 mg of lactoferrin per kg of body weight is administered (paragraph [0038]; corresponding to 0.6 mg to 1.2 g per day assuming single dose/day and body weight of 60 kg; claims 18 and 19). Since Kruzel *et al.* teach the same effective amount of lactoferrin (e.g., 0.6 mg to 1.2 g per day, which is in the range of 1 ng to 100g per day used in the claimed method, see paragraph [0073] of US 2004/0151784 (10/733,621)) is used for improvement of overall wellness (paragraph [0046]) in the treatment of MS patients, the administration of lactoferrin would inherently provide an improvement in the pain associated with MS (claims 1 and 3). Although Kruzel *et al.* do not specifically indicate lactoferrin reduces the production or activity of pro-inflammatory cytokines (e.g., TNF-α), or enhances the production or activity of certain cytokines (e.g., IL-18), the reference teaches the same method step (the administration of lactoferrin) as the claimed invention, where the lactoferrin would be expected to produce these effects (claims 20-22).

Response to Arguments

Applicants indicate that independent claim 1 has been amended to recite pain being associated with cancer, disorders of the central nervous system or surgery, which is not taught or suggested in Kruzel *et al.*; and Kruzel et al. do not identify, mention or suggest the use lactoferrin to treat pain is associated with cancer, disorders of the central nervous system or surgery (pages 6-7 of the response).

Applicant's response has been fully considered, however, the argument is not found persuasive because Kruzel *et al.* teach using the same method step for improvement of overall wellness in the treatment of MS patients (a disorders of the central nervous system), where the administration of lactoferrin would inherently provide an improvement in the pain associated with MS. Therefore, the claimed method is anticipated by the reference.

New Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Olmarker *et al.* (WO 02/080891, October 17, 2002) in view of Hanson *et al.* (WO 00/01730, January 13, 2000).

Olmarker *et al.* teach the use of a TNF inhibitor (e.g., lactoferrin and peptides derived from lactoferrin disclosed in WO 00/01730; page 8, lines 1-3) for the production of a pharmaceutical composition for the treatment of low back pain, where the low back pain may be the result of unknown causes (idiopathic) or may be related to various kinds of spine trauma,

including whiplash injury (page 5, line 34-page 6, line 13); the pharmaceutical composition is administered parenterally, orally, or topically in a therapeutically effective amount to an improvement of the patient's condition, and may comprise an inert vehicle or pharmaceutically acceptable carriers. However, Olmarker *et al.* do not specifically identify the peptides derived from lactoferrin being N-terminal lactoferrin variant.

Hanson *et al.* teach the peptides derived from N-terminal end of lactoferrin, e.g., the peptides have 14 amino acid residues and corresponds to residues 18-31 of human lactoferrin with some alterations, e.g., C-20 is replaced by A, Q-22 is replaced by K, and N-26 is replaced by D, which have the same and better properties (page 3, lines 10-24).

At the time the invention was made, it would have been obvious that a person of ordinary skill in the art is motivated to use the N-terminal lactoferrin variant as taught by Hanson *et al.* to prepare a lactoferrin composition for the treatment of low back pain as indicated by Olmarker *et al.* (claims 35 and 36) because the new peptides resemble human lactoferrin but they are easier and cheaper to produce, and are essentially as efficient as human lactoferrin in the treatment (page 3, lines 3-9 of Hanson *et al.*). Thus, the combined references result in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

Response to Arguments against Old Claims 33 and 34

Applicants indicate that independent claim 1 has been amended to recite pain being associated with cancer, disorders of the central nervous system or surgery, which is not taught or suggested in Olmarker *et al.* nor Hanson *et al.*; and neither Olmarker *et al.* nor Hanson *et al.* identify, mention or suggest the use lactoferrin to treat pain is associated with cancer, disorders of the central nervous system or surgery (page 7 of the response).

Applicant's response has been fully considered, however, the argument is not found persuasive because independent claim 35 recites a method of treating a subject suffering from pain as shown in the old claims 33 (acute pain) and 34 (chronic pain), claim 35 does not recite a method of treating pain associated with cancer, disorders of the central nervous system or surgery. The combination of Olmarker *et al.* and Hanson *et al.* teach using the N-terminal lactoferrin variant to treat low back pain. Therefore, it would be prima facie obvious that the combined references teach the claimed method.

New-Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1, 3-22 and 35-37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 and 12 of copending Application No. 10/862,213 (now available as PGPub US 2005/0019342). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 3-22 and 35-37 in the instant application disclose a method of treating a subject suffering from pain comprising administering to the subject an effective amount of a lactoferrin composition to provide an improvement in pain in the subject, wherein the pain is associated

with cancers, disorders of the central nervous system or surgery; or a method of treating a subject suffering from pain comprising administering to the subject an effective amount of a lactoferrin composition consisting essentially of N-terminal variant to provide an improvement in pain in the subject. This is an obvious variation in view of claims 1-8 and 12 in the copending application which disclose a method of treating cancer comprising administering to a subject a cancer immunotherapy and an adjuvant, wherein said adjuvant is a lactoferrin composition that is administered in an amount sufficient to provide improvement in the cancer in the patient; and the specification discloses the lactoferrin composition comprises lactoferrin or an N-terminal lactoferrin variant (paragraph [0009]), where the N-terminal lactoferrin variant mediates the same biological activity as full-length lactoferrin, e.g., stimulating the production of various cytokines (e.g., IL-18) and inhibits the production of various pro-inflammatory cytokines (e.g., TNF-α), and improves parameters which promote or enhance the well-being of subject with respect to the medical treatment of cancer, e.g., a decrease in pain to the subject that can be attributed to the subject's condition (paragraphs [0043], [0059]); and the lactoferrin composition can be administered orally, parentally or topically, for oral administration, an antacid can be administered in conjunction with the lactoferrin composition (paragraph [0012]). Both the claims of instant application and the claims of the copending application are directed to a method of treating a patient suffering from cancer comprising administering an effective amount of a lactoferrin composition to provide improvement in the cancer of the patient such as the pain associated with cancer. Thus, claims 1, 3-22 and 35-37 in present application and claims 1-8 and 12 in the copending application are obvious variations of a method of treating a patient suffering

from cancer comprising administering an effective amount of a lactoferrin composition to provide improvement in the cancer of the patient such as the pain associated with cancer.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

10. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D. CMK
Patent Examiner

CMK
June 29, 2005

KATHLEEN KERR, PH.D.
PRIMARY EXAMINER
SPE